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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,379	07/06/2001	Hing C. Wong	44470 C1-CPA-C (71758)	4293

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EXAMINER
VANDER VEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/01/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/900,379	Applicant(s) WONG ET AL.	
	Examiner F. Pierre VanderVegt	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

Claims 1-50 have been canceled previously.

Claims 51-59 are currently pending and are the subject of examination in the present Office Action.

Priority.

1. This application is a continuation of U.S. Application Serial Number 08/776,084, which is a continuation-in-part of U.S. Application Serial Number 08/382,454, which is a continuation-in-part of U.S. Application Serial Number 08/283,302.

In view of Applicant's response of April 14, 2003, Applicant's claim of priority to the above-mentioned applications.

Applicant should amend page 1 of the specification to update the priority information.

Response to Arguments

2. Applicant's arguments with respect to claims 51-59 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

3. Claims 51-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 is ambiguous and unclear as to whether the alpha and beta chains must be derived from the same MHC molecule. Is it applicant's intention to claim a MHC II:peptide fusion protein in which the MHC domains that are linked together are derived from different MHC alleles or is it applicant's intention to claim a MHC II:peptide in which the MHC domains are all derived from the same MHC molecule? All dependent claims are included in this ground of rejection.

Claim 51 is ambiguous and unclear as to whether the individual MHC molecules which compose the multivalent MHC molecule are the same or different. Does each MHC molecule of the complex

present an identical peptide, or do they possess different binding grooves and present different peptides? All dependent claims are included in this ground of rejection.

Claim 51 is unclear regarding the effect of the multivalent MHC molecules on the development of T cells. Claim 51 recites "increasing or decreasing T cell...development." Development of a T cell is not a property which can be "increased" or "decreased" and Applicant should clarify how development of T cells is affected by the composition of the claim.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 51 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892).

The '422 patent discloses MHC Class II fusion complexes comprising an antigen binding site that contain a presented peptide (see column 4, lines 48-55, in particular). The antigen binding site disclosed by '422 patent is the same MHC peptide binding groove taught by the instant application on page 2, lines 4-6. The '422 patent further discloses that the peptide portion in the context of MHC Class II molecule will modulate the activity of a T cell (see column 12, lines 36-45, in particular). The '422 Patent also discloses that peptide and the MHC Class II molecule can be covalently linked (see column 4, lines 58-59, in particular) or that the peptide and MHC molecule may be linked via peptide linkage (see Column 13, 45-47, in particular). The '422 patent further discloses that the MHC Class II molecule may be terminally truncated to delete the transmembrane and cytoplasmic domains (see Figure 1 and Column 6, lines 32-60 and Column 7, lines 1-5, and Column 19, lines 35-45, in particular). The '422 patent also discloses that the presenting peptide may be attached to the N-terminal end of the MHC Class II molecule (see column 13, lines 17-31, in particular). The '422 Patent also discloses that the peptide and MHC molecule may be linked via peptide linkage (see Column 13, 45-47, in particular).

The claimed invention differs from the '422 patent only by the use of MHC Class II fusion complex molecules that are multivalent. However, McCluskey teaches that MHC Class I fusion complexes can be made multivalent by coupling to dextran or agarose beads or by adsorption to polystyrene and that only multivalent preparations stimulate T cells (see abstract, page 1452, left column, second and third paragraphs, and page 1454, left column, last paragraph, in particular).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make multivalent MHC Class II-peptide conjugates using the same methods taught by McCluskey for the purpose of enhancing T cell binding avidity of MHC Class II:peptide fusion molecules.

5. Claims 52 and 53 are rejected under 35 U.S.C. 103(a)) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892) as applied to claim 51 above, and further in view of WO 93/10220 (BB form PTO-1449).

The '422 patent and McCluskey have been discussed supra. The claimed invention differs from the prior art of record only by linking the multivalent MHC molecules to an immunoglobulin. WO 93/10220 teaches chimeric proteins comprising an MHC component linked to an immunoglobulin constant region component and that the MHC component preferably consists of the extracellular portion of a MHC II protein (see abstract, Figures 2-3, page 3 and Claim 1, in particular). WO 93/120220 teaches that the chimeric proteins can be used to modulate the activity of T cells, such as inducing anergy (see page 9, lines 14-22, and claim 12, in particular). WO 93/10220 also teaches that the chimeric molecules may comprise a single chain MHC molecule linked to immunoglobulin heavy chain. WO 93/10220 also teach multivalent MHC-Ig chimeric protein which comprise MHC molecule that contains a peptide binding groove linked to each of two Ig heavy chain components (see Figure 2, in particular). Therefore it would have been prima *facie obvious* to one with ordinary skill in the art at the time of the invention to modify the MHC-Ig chimeric protein taught by WO 93/10220 by linking the presenting peptide to the multivalent MHC molecule as taught by the combination of the '422 patent and McCluskey with a reasonable expectation that the resulting fusion complex could be used to downregulate the immune response to the presented peptide.

6. Claims 55-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892) as applied to claim 51 above, and further in view of US Patent 5,338,532 to Tomalia et al (A1 form PTO-892)

The '422 patent and McCluskey have been discussed supra. The claimed invention differs from the prior art teachings only by use of multivalent MHC fusion molecules chemically linked by a dendrimer particle.

The '532 patent discloses the use of dendrimers as carriers for immuno-potentiating agents to allow for control of the size, shape and surface composition of the conjugate (see column 9, lines 23-54, in particular). The '532 patent further discloses that the dendrimers may be chemically linked to the ligand (see column 13, line 44 through column 16, line 6, in particular). The '532 patent further discloses that use of dendrimers as carriers allows the optimization of antigen presentation to an organism. Therefore it would have been prima facie obvious to one with skill in the art at the time of the invention to substitute dendrimers for the dextran or agarose beads used by McCluskey in the preparation of multivalent MHC fusion molecule taught by the '422 Patent and McCluskey with the expectation that the multivalent MHC fusion molecule chemically linked by a dendrimer particle would have enhanced T cell binding avidity.

Conclusion

7. No claim is allowed.

8. In view of the new grounds of rejection, this action is made **NON-FINAL**.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00 ET; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014.Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D
Patent Examiner
June 30, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CEN TER 1600
6/30/03